REMARKS

I. Status of the Claims

By this amendment, claims 1, 14, 15, and 32 are amended and claim 55 is added. Upon entry of this Amendment, claims 1-55 will be pending.

Exemplary support for the amendments to claims 1, 14, 15, and 32 is found throughout the specification. *See* page 1, line 20. Exemplary support for claim 55 is found on page 2, lines 24-32. Claim 55 is added to more clearly define claim scope.

Because the foregoing amendments to not add new matter, entry thereof by the Examiner is respectfully requested.

It is acknowledged that the Examiner notes that claims 36-42 are free of the prior art and that claims 23-30, 32-35, 47, and 48 would be allowable if written in independent form including all of the limitation of the base claim and any intervening claims.

II. Claim Rejections - 35 U.S.C. § 103

A. Rejection Of Claims 1-10, 22, And 49-54 As Being Allegedly Obvious Over Knudsen et al. In View Of Makino et al.

Claims 1-10, 22, and 49-54 are rejected by the Examiner under 35 U.S.C. § 103 as being allegedly obvious over Knudsen et al. (WO 99/43361) ("Knudsen") in view of Makino et al. (U.S. Patent No. 4,985,244) ("Makino"). The Examiner asserts that although Knudsen fails to disclose using histidine as a stabilizing agent in a pharmaceutical composition, the claimed invention would have been obvious to a person of ordinary skill in the art at the time the invention was made because Makino disclose using 5% (w/v%) of histidine as a stabilizing agent in a vaccine composition. Applicant respectfully traverses and requests reconsideration and withdrawal of the rejection.

A proper rejection for obviousness under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, or device, or carry out the claimed process, and

(2) whether the prior art would also have revealed that in making or carrying out the claimed invention, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art, and not in the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991). In the present case, the examiner has failed to establish a *prima facie* case of obviousness for the following reasons.

1. There is no Motivation to Combine the Teachings of Makino and Knudsen

There is no teaching or suggestion in the cited prior art to combine the teachings of Makino with the teachings of Knudsen to obtain the claimed invention because the two references are directed to different types of compositions which are not interchangeable, and which have different properties and characteristics.

Specifically, Knudsen teaches a pharmaceutical composition comprising a GLP-2 derivative of improved solubility and/or stability. GLP-2 and derivatives thereof are peptides. In contrast, Makino teaches a stabilized live attenuated vaccine. A peptide is defined as "two or more amino acids joined by a peptide bond" (see attached definition from http://www.genome.gov/glossary.cfm?key=peptide). In contrast, a vaccine is defined as "a suspension of attenuated or killed microorganisms (bacteria, viruses or rickettsiae), administered for the prevention, amelioration, or treatment of infectious diseases" (see attached definition from http://cancerweb.ncl.ac.uk/cgi-bin/omd?vaccine).

While a peptide is a compound formed by joining amino acids, a vaccine comprises complex attenuated or killed organisms. Since a peptide is entirely different from a vaccine, a person of ordinary skill in the art would not expect the stability of a vaccine in a solution to have any bearing on the stability of a peptide in the same solution. Therefore, the cited references lack the requisite teaching or suggestion to motivate a person of ordinary skill in the art to combine the references. Moreover, the Examiner has failed to provide any reasoning to support the assertion that a person of ordinary skill in the art would have been motivated to combine the teachings of the cited art to obtain the claimed invention.

2. One of Ordinary Skill in the Art Would Not Have had a Reasonable Expectation of Success in Obtaining the Claimed Invention by Combining the Teachings of Makino and Knudsen

A person of ordinary skill in the art would not have had a reasonable expectation of success in adding a stabilizing agent known to stabilize vaccine solutions to a pharmaceutical composition comprising a GLP-2 peptide derivative. As discussed above, a peptide is entirely different from a vaccine. Thus, a person of ordinary skill in the art would not expect that a stabilizer known to stabilize vaccines would also stabilize a pharmaceutical composition comprising a GLP-2 peptide derivative.

In particular, Applicant directs the Examiner's attention to page 5 of the March 8, 2002, Office Action for the present application where the Examiner stated that Knudsen and Makino do not teach the claimed invention because "it is not known whether histidine can stabilize GLP-2 or its analogs in the GLP-2 formulation."

For the above reasons, the Examiner has failed to establish a *prima facie* case of obviousness for the rejection of the claims over Knudsen in view of Makino. Withdrawal of this ground for rejection is respectfully requested.

B. Rejection Of Claims 11, 12, And 31 As Being Allegedly Obvious Over Knudsen In View Of Makino, And Further In View Of Hora et al.

Claims 11, 12, and 31 are rejected by the Examiner as being allegedly unpatentable over Knudsen in view of Makino, as applied to claims 1-10 above, and further in view of Hora et al. (U.S. Patent No. 5,997,856) ("Hora"). Applicant respectfully traverses this ground for rejection.

As discussed above, the Examiner has failed to establish a *prima facie* case of obviousness for the rejection of the claims over Knudsen in view of Makino. Hora does not remedy the deficiencies of Knudsen and Makino. Therefore, claims 11, 12, and 31 are not obvious over Knudsen in view of Makino and further in view of Hora. Applicant respectfully traverses and requests reconsideration and withdrawal of the rejection.

C. Rejection Of Claims 13-15 And 17-20 As Being Allegedly Obvious Over Knudsen In View Of Makino, And Further In View Of Drucker et al.

Claims 13-15 and 17-20 are rejected by the Examiner as being allegedly unpatentable over Knudsen in view of Makino, as applied to claim 1 above, and further in view of Drucker et al. (WO 97/39032) ("Drucker A"). Applicant respectfully traverses this ground for rejection.

As discussed above, the Examiner has failed to establish a *prima facie* case of obviousness for the rejection of the claims over Knudsen in view of Makino. Drucker does not remedy the deficiencies of Knudsen and Makino. Therefore, claims 13-15 and 17-20 are not obvious over Knudsen in view of Makino and further in view of Drucker. Applicant respectfully traverses and requests reconsideration and withdrawal of the rejection.

D. Rejection of claims 16 and 21 As Being Allegedly Obvious Over Knudsen In View Of Makino, And Further In View Of Thim et al.

Claims 16 and 21 are rejected by the Examiner as being allegedly unpatentable over Knudsen in view of Makino, as applied to claim 1 above, and further in view of Thim et al. (U.S. Patent No. 5,912,229) ("Thim"). Applicant respectfully traverses this ground for rejection.

As discussed above, the Examiner has failed to establish a *prima facie* case of obviousness for the rejection of the claims over Knudsen in view of Makino. Thim does not remedy the deficiencies of Knudsen and Makino. Therefore, claims 16 and 21 are not obvious over Knudsen in view of Makino and further in view of Thim. Applicant respectfully traverses and requests reconsideration and withdrawal of the rejection.

E. Rejection Of Claims 43-46 As Being Allegedly Obvious Over Knudsen In View Of Makino, And Further In View Of Drucker et al.

Claims 43-46 are rejected by the Examiner as being allegedly unpatentable over Knudsen in view of Makino as applied to claim 1 above, and further in view of Drucker et al.

(U.S. Patent No. 5,952,301) ("Drucker B"). Applicant respectfully traverses this ground for rejection.

As discussed above, the Examiner has failed to establish a *prima facie* case of obviousness for the rejection of the claims over Knudsen in view of Makino. Drucker B does not remedy the deficiencies of Knudsen and Makino. Therefore, claims 43-46 are not obvious over Knudsen in view of Makino and further in view of Drucker B. Applicant respectfully traverses and request reconsideration and withdrawal of the rejection.

CONCLUSION

As the above-presented amendments and remarks address and overcome all of the rejections presented by the Examiner, withdrawal of the rejections and allowance of the claims are respectfully requested.

If the Examiner has any questions concerning this application, he or she is requested to contact the undersigned.

Respectfully submitted,

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By Michele M. Simkin

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A glucagon-like peptide-2 (GLP-2) formulation comprising:

(a) a medically useful amount of a naturally occurring GLP-2 peptide or an analog thereof;

(b) a phosphate buffer in an amount sufficient to adjust the pH of the formulation to a physiologically tolerable level;

(c) L-histidine; and

(d) a bulking agent selected from the group consisting of mannitol and sucrose.

14. (Amended) The GLP-2 formulation of claim 13, wherein the GLP-2 peptide has the sequence of a GLP-2 species from [n] an animal selected from the group consisting of a primate, rat, mouse, porcine species, oxine species, bovine species, degu, hamster, guinea pig, fish, chicken, and human.

15. (Amended) The GLP-2 formulation of claim 14, wherein the GLP-2 peptide is [h[Gly2]GLP-2] h(Gly2)GLP-2.

32. The GLP-2 formulation of claim 31, wherein the GLP-2 is [h[Gly2]GLP-2] h(Gly2)GLP-2.